*Postgrad Med J* 1995; **71**: 457–465 

*Classic therapies revisited*

# Cardioversion of atrial fibrillation

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**Summary**

**Cardioversion to sinus rhythm should be considered for all patients in atrial fibrillation in order to improve cardiac performance and perhaps to reduce the long-term risk of thromboembolic complications. Different methods of cardioversion, whether electrical or pharmacological, exist and there is often uncertainty about performing the procedure. In particular, there is often confusion about the use of anti-arrhythmic drugs and the suitable length of anticoagulant therapy required pre- and post-cardioversion. This review discusses the current understanding of electrical and pharmacological cardioversion of atrial fibrillation, the clinical effects and the role of prophylactic anti-arrhythmic and anticoagulant therapy in this procedure.**

**Keywords**: cardioversion, atrial fibrillation, anticoagulant therapy

**Atrial fibrillation**

- the commonest sustained disorder of cardiac rhythm
- relatively uncommon under the age of 50 years but found in 0.5% of people aged 50–59 years, increasing to 8.8% at 80–89 years
- present in 6–7% of acute medical admissions to a district general hospital
- may be either chronic or paroxysmal

**Box 1**

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Accepted 19 April 1995

Atrial fibrillation is an arrhythmia which is associated with an increased risk of thromboembolism and haemodynamic disturbance. Instead of continuing in a potentially serious cardiac arrhythmia (which is associated with an increased mortality, a five-fold risk of stroke and other major thromboembolic complications) and the requirement for drug therapy with potential adverse effects (including oral anticoagulants and anti-arrhythmic therapy), cardioversion from atrial fibrillation to sinus rhythm should be considered for suitable patients. The potential benefits of a return to sinus rhythm include an improvement in patient well-being and exercise capability (secondary to the return of atrial filling, and consequent improved cardiac output), the avoidance of (potentially dangerous) drug therapy and perhaps a reduction in stroke and thromboembolic risk.

However, in surveys of the management of patients with atrial fibrillation,[1] there has generally been a low proportion of patients considered for cardioversion. This may be a reflection of perceived risk of the procedure, the associated thromboembolic risk and the uncertainty of patient selection. In addition, if cardioversion is undertaken, there is also uncertainty about the procedure, whether electrical or pharmacological, and the suitable length of anticoagulant therapy required pre- and post-cardioversion.

## General pathophysiology

With increasing age and any (progressive) impairment of left ventricular contraction, the dependence on atrial function increases and atrial systole contributes an increasing amount towards overall stroke volume. In atrial fibrillation, the haemodynamic disturbances result essentially from the absence of atrial systole and from the rapidity and irregularity of the ventricular response.

The lack of organised atrial mechanical activity in atrial fibrillation results in a concomitant decrease in stroke volume and cardiac output. The loss of atrial systole also results in blood stasis within the atria, a condition which favours thrombus formation (thrombogenesis). In addition, sudden changes to a very rapid heart rate in atrial fibrillation may significantly reduce the diastolic filling interval, resulting in a further reduction in cardiac output. This will have particular importance in the presence of either valvular stenosis or reduced left ventricular compliance (for example, in left ventricular hypertrophy).[2] The onset of a rapid ventricular response may also lead to a degree of mitral incompetence thus further reducing forward flow.[2]

These deleterious haemodynamic changes of atrial fibrillation have been substantiated by numerous studies showing a significantly improved functional or exercise capacity and increased cardiac output following cardioversion of atrial fibrillation to sinus rhythm.[3,4] Cardioversion from atrial fibrillation to sinus rhythm may therefore have distinct haemodynamic advantages.

## Electrical and pharmacological cardioversion

Cardioversion of atrial fibrillation can be performed electrically, by means of a synchronous direct current discharge, or pharmacologically, by the use of a suitable anti-arrhythmic drug.

### ELECTRICAL CARDIOVERSION

Electrical cardioversion works by repolarising the errant atrial conduction, restoring ordered conduction. During the initial asystolic period, the sino-atrial node rapidly resumes its role as cardiac pacemaker. Although external electrical cardioversion is effective in restoring sinus rhythm, this efficacy can range from 20 to 90% of patients, with the procedure being highly influenced by the underlying aetiology.[5] The highest recorded success rates for cardioversion are seen in patients with atrial fibrillation secondary to hyperthyroidism, whilst the lowest rates are seen in patients with severe mitral regurgitation.[5] Attention to proper technique for external cardioversion will greatly improve efficacy.[6]

Another method of electrical cardioversion is the transoesophageal method,

**Aetiological factors**

*Cardiac causes*
- ischaemic heart disease
- rheumatic heart disease
- hypertension
- sick sinus syndrome and pre-excitation syndromes (eg, Wolff Parkinson White)
- cardiomyopathy or heart muscle disease
- pericardial disease, including effusion, constrictive pericarditis

*Noncardiac causes of atrial fibrillation*
- acute infections, especially pneumonia
- lung carcinoma
- other intrathoracic pathology, eg, pleural effusion
- alcohol excess
- postoperative, especially after thoracotomy or coronary artery bypass surgery
- pulmonary thromboembolism
- thyrotoxicosis

*Idiopathic or 'lone' atrial fibrillation*

**Box 2**

**Complications of atrial fibrillation**

- haemodynamic effects, including heart failure and decreased exercise tolerance
- stroke and thromboembolism
- increased mortality five-fold
- requirement for long-term anticoagulant and anti-arrhythmic therapy, with potential adverse effects

*Cardioversion of atrial fibrillation to sinus rhythm avoids some of these adverse features*

**Box 3**

**Management options**

- is it atrial fibrillation? If so, is it chronic or paroxysmal?
- full clinical assessment, including echocardiography
- antithrombotic therapy: aspirin for low-risk patients but warfarin required for most patients, especially if cardioversion is to be attempted
- consider whether rate control of atrial fibrillation or cardioversion appropriate
- if cardioversion, decide whether to attempt electrical or pharmacological cardioversion (using Class I or III drugs) and whether the use of anti-arrhythmic therapy post-cardioversion is appropriate. Anticoagulation should be maintained post-cardioversion for at least four weeks

**Box 4**

which has recently been compared to transthoracic cardioversion in a randomised trial.[7] Transoesophageal cardioversion was more successful than transthoracic cardioversion at low energies ($\leqslant$ 100 Joules) with a success rate of 72%, compared with 34% for transthoracic cardioversion; lower median energies were required (180 J *vs* 350 J, respectively), with few complications.[7] In patients who failed external cardioversion, internal cardioversion (using electric shocks delivered within the right atrium) is a specialist technique recently described.[8] In a recent randomised comparison of external and internal cardioversion of chronic atrial fibrillation, the efficacy of internal cardioversion was found to be significantly greater than that of external cardioversion (91% *vs* 67%, respectively).[8]

Despite the high initial success rates for electrical cardioversion, there is often a high rate of reversion to atrial fibrillation without the concomitant use of an anti-arrhythmic agent.[7] In resistant cases of atrial fibrillation, amiodarone pre-loading can increase the chances of successful cardioversion.[9]

## PHARMACOLOGICAL CARDIOVERSION AND ANTI-ARRHYTHMIC THERAPY

A popular alternative to electrical cardioversion is pharmacological (or chemical) cardioversion, especially in patients with atrial fibrillation of recent onset. In general, drugs that are usually used to maintain sinus rhythm after electrical cardioversion, such as Class I and Class III anti-arrhythmic drugs, are also effective for pharmacological cardioversion.

The Class I drugs which are most commonly in use are quinidine, flecainide and propafenone. Other similar drugs used in cardioversion and the maintenance of sinus rhythm include disopyramide and procainamide, although the efficacy of these drugs is lower.[10,11] Quinidine remains a frequently used Class Ia drug for cardioversion and the maintenance of sinus rhythm post-cardioversion. It has been shown to be very effective in patients with lone atrial fibrillation, but adverse effects were reported in 22% of patients, requiring drug discontinuation in 15%.[12] The efficacy of quinidine is supported by a meta-analysis of six controlled trials which have shown that patients treated with quinidine were less likely to have a recurrence of atrial fibrillation.[13] Importantly, however, this analysis also demonstrated an excess of mortality for the treated group.

Both flecainide and propafenone are effective drugs in the cardioversion of atrial fibrillation, with a success rate between 25–55% when given orally.[10,14] Several studies of flecainide have shown its efficacy in cardioversion (in up to 92% of patients, if given intravenously) and in preventing the recurrence of the arrhythmia.[11,15,16] However, the drug has no rate-limiting properties, and has been reported to cause adverse effects in 74% of patients, although these were mostly tolerable.[15,16] Propafenone, another Class Ic compound, may potentially be more useful than flecainide as it has inherent rate-limiting (Class II) properties, thus allowing greater ventricular rate control. In one study, however, flecainide was found to be more effective than propafenone in converting patients to sinus rhythm (with a 90% *vs* 55% conversion rate to sinus rhythm, respectively).[17] Propafenone has been compared to sotalol, and both are equally effective in maintaining sinus rhythm in such patients.[18]

There is a general concern regarding an increased risk of mortality with the use of Class I anti-arrhythmics, especially in the Cardiac Arrhythmia Suppression Trial, in which post-myocardial infarction patients given flecainide to control ventricular arrhythmias, had a worsened prognosis.[19] The risks to patients with atrial fibrillation and other supraventricular arrhythmias, especially in those with underlying coronary artery disease and impaired cardiac function, are not entirely known. An initial report for flecainide and encainide in patients with supraventricular arrhythmias is encouraging, with no excess mortality demonstrated, although cardiac function was not specified and heart disease was present in only 45% of those taking encainide and 58% of those taking flecainide.[20]

Amiodarone, a Class III anti-arrhythmic drug, has been shown to be highly effective in the cardioversion of atrial fibrillation, even in previously refractory cases; and in maintaining this effect long-term, where it is more effective than either verapamil or quinidine.[21,22] The drug can be used both orally and intravenously; oral administration has a slow onset of action due to the long half-life of the drug, while intravenous amiodarone may act relatively rapidly. Intravenous amiodarone has been shown to restore sinus rhythm in up to 75% of cases, where its efficacy is comparable to electrical cardioversion.[23–25] In cases of resistant atrial fibrillation, a four-week loading of amiodarone pre-cardioversion (at a dose of 600 mg/day) and a low-dose (on average 200 mg/day) maintenance regime following successful cardioversion was effective in achieving cardioversion and sustaining sinus rhythm.[9] However, the use of amiodarone has to be moderated by its potentially serious, albeit relatively rare, side effects.[26] These are more common with higher doses of amiodarone (16.7%, compared with

**Cardioversion of atrial fibrillation – how to do it**

- admit patient to hospital for ECG monitoring (eg, coronary care unit)
- serum electrolytes (especially potassium) should be normal
- ensure anticoagulation is adequate, with no evidence of digitoxicity, the drug can be taken up to the day before the procedure. Serum digoxin levels should be checked if digitoxicity is suspected and the procedure delayed.

*Pharmacological cardioversion*
- infusion of anti-arrhythmic drug (eg, flecainide, amiodarone) should be started under continuous ECG monitoring

*Electrical*
- patient should be fasted
- short general anaesthetic required to eliminate discomfort associated with the transthoracic shock. Resuscitation equipment should be available. ECG and blood pressure monitoring, and pulse oximetry is desirable (see figure 1)
- synchronised DC shock is given, starting at 100 Joules, with intermediate 'step-ups', eventually to 360 Joules
- after the procedure, the patient is monitored for at least 1 hour to ensure stability of rhythm and blood pressure

**Box 5**

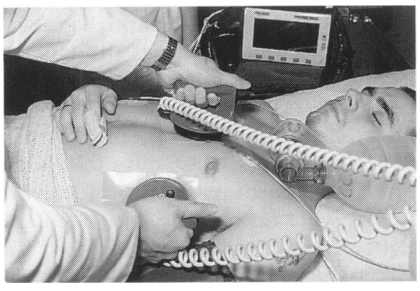

**Figure 1** The procedure of cardioversion (see box 5 for discussion of equipment)

5.4% with low-dose regimes) and with prolonged therapy, although side effects may be reversible on withdrawal of the drug.[26] Amiodarone can also have important drug interactions. For example, it can lead to over-coagulation in patients taking warfarin, perhaps by a hepatic interaction.[27] It can also significantly increase the plasma concentrations of digoxin, thereby leading to potential toxicity.

Whilst occasionally effective in converting atrial fibrillation to sinus rhythm, verapamil has a much lower rate of conversion than that reported for amiodarone, flecainide or propafenone.[17,22,28] It should be noted that digoxin is no better than placebo for the attempted restoration of sinus rhythm.[29] There is also no evidence that digoxin is effective as prophylaxis against recurrence of atrial fibrillation after cardioversion. In contrast, in patients with recurrent atrial fibrillation, paroxysms of atrial fibrillation occurred more frequently, for significantly longer and were faster in patients receiving digoxin.[30,31] The mechanisms for this is unclear but digoxin increases vagal tone and reduces the atrial refractory period thus paradoxically rendering the atrium more susceptible to fibrillation. This may reduce or even prevent the chance of reversion to sinus rhythm.[30]

## Thromboembolism, antithrombotic therapy and cardioversion

Another important therapeutic consideration during cardioversion of atrial fibrillation (whether pharmacological or electrical) is the use of prophylactic anticoagulation to reduce the risk of stroke and thromboembolism following cardioversion. It is estimated that peripheral emboli may complicate external cardioversion in 1–3% of cases.[5] Thromboembolism following pharmacological cardioversion may well have similar rates.[32]

Anticoagulant therapy is therefore advised, despite the absence of prospective randomised trials on the effectiveness of such therapy, in the cardioversion of such patients. However, why these patients should develop thromboembolism is only appreciated by an understanding of the underlying mechanisms and factors promoting thromboembolism during cardioversion.

### MECHANISMS AND FACTORS CONTRIBUTING TO THROMBOEMBOLISM

The mechanisms and factors contributing to thromboembolism following cardioversion of atrial fibrillation remain to be clearly defined and various possibilities have been suggested.

Firstly, a mechanical explanation for thromboembolism after cardioversion has been suggested. The sudden resumption of mechanical atrial systolic function may result in the embolisation of any pre-existing clot formed within the left atrium, which is dislodged by the effect of a change in cardiac rhythm during cardioversion. However, the minimum time for such thrombi to form in the fibrillating atria is as yet unknown.[33] As the time for the return of atrial systole is variable between individual patients, and can take up to three weeks post-cardioversion,[34] anticoagulant therapy post-cardioversion should at least be continued until the return of atrial systolic function. In addition, it has been suggested that the procedure of cardioversion may actually promote new thrombus formation due to transient atrial dysfunction ('stunning').[35] The latter leads to the new development of spontaneous echo contrast on transoesophageal echocardiography and thromboembolic complications, even in the absence of demonstrable left atrial thrombus.[35] However, if atrial dysfunction simply reflects the process of cardioversion, it does not explain why atrial recovery is dependent upon the preceding duration of atrial fibrillation. In addition, if the rhythm change from atrial fibrillation to sinus rhythm is the critical factor for thromboembolism, this does not adequately explain the supposed lower rate of thromboembolic complications in patients with paroxysmal atrial fibrillation.

It has been argued that the duration of atrial fibrillation is important as recently formed, poorly adherent thrombus is more likely to dislodge at the time of cardioversion, compared with older thrombus which is likely to more firmly adherent.[33] An estimate of the time required for this infilterative process is approximately 14 days, so anticoagulation for this time period might prevent new clot formation and allow the most recently formed thrombi to become sufficiently adherent.[33] However, this time period cannot be precisely defined and is likely to vary according to the haemodynamic status, atrial size and underlying atrial pathology, together with the effectiveness of anticoagulation.

Abnormalities in haemorheological function and prothrombotic markers intrinsic to atrial fibrillation may also contribute to the thromboembolic risk post-cardioversion. Indeed, patients with chronic atrial fibrillation have abnormalities in clotting factor levels.[36,37] Atrial fibrillation is also associated with elevated levels of atrial natriuretic peptide, which may contribute to

**Pharmacological cardioversion of atrial fibrillation**

Some properties of commonly prescribed drugs

*Digoxin*
- useful for rate control at rest, but not the ventricular response with exercise
- detrimental in paroxysmal atrial fibrillation
- no use for cardioversion or for the maintenance of sinus rhythm post cardioversion

*Verapamil or diltiazem*
- useful for rate control even with exercise
- useful if atrial fibrillation associated with ischaemic heart disease, hypertension or hypertropic cardiomyopathy
- less effective if used for cardioversion or maintenance of sinus rhythm

*Class I anti-arrhythmics (quinidine, flecainide, propafenone)*
- useful for paroxysmal atrial fibrillation, cardioversion to sinus rhythm and the maintenance of sinus rhythm post-cardioversion
- do not use if underlying left ventricular dysfunction and significant ischaemic heart disease

*Class III anti-arrhythmics (amiodarone, sotalol)*
- useful for paroxysmal atrial fibrillation, cardioversion to sinus rhythm and the maintenance of sinus rhythm post-cardioversion
- amiodarone is useful if underlying left ventricular dysfunction but side effects are common
- sotalol is effective and well-tolerated; also has beta-blocker properties and useful if concomitant ischaemic heart disease or hypertension

**Box 6**

haemoconcentration, a raised haematocrit and subsequent thromboembolism and stroke.[38] If the mechanisms of thromboembolism are not simply mechanical but related to an underlying prothombotic state, measurement of suitable markers of thrombogenesis may be useful in identifying 'high risk' patients and determining the duration and intensity of anticoagulant therapy required. However, a prothrombotic state is unlikely to be the sole mechanism, as it is also recognised that there may be an increased risk of thromboembolism around the time of onset of atrial fibrillation.

Another factor which may influence the mechanism of thromboembolism with cardioversion is the left atrial size. Left atrial enlargement is also associated with increased spontaneous echo contrast on transoesophageal echocardiography, suggesting slow or sluggish blood flow within the enlarged atrial cavity.[39,40] The rheological mechanism for spontaneous echo contrast is thought to involve the presence of fibrinogen, or its products, and red cell aggregation or rouleau formation,[41,42] thus providing a 'link' between haemorheological abnormalities and visual demonstration of flow abnormalities within the left atrium, continuously in chronic atrial fibrillation, and intermittently in paroxysmal atrial fibrillation.[43]

Finally, abnormalities in cerebral blood flow may be part of the mechanism for thromboembolic stroke following cardioversion. For example, there appears to be increased cerebral blood flow after cardioversion from atrial fibrillation to normal sinus rhythm, and this may predispose to cerebral embolism in the distribution of the middle cerebral artery.[44,45]

## THE ROLE OF ANTICOAGULATION

The role of prophylactic anticoagulation in certain patients with chronic atrial fibrillation is now well-established, with evidence from large randomised trials.[46] However, the role of prophylactic anticoagulation to prevent thromboembolism following cardioversion, for patients in atrial fibrillation, has not been as intensely investigated. Consequently, there is a lack of consensus regarding the need for (and the duration of) such therapy before the procedure is undertaken.

The role of prophylactic anticoagulation has been clinically examined in several large series. Bjerkelund and Orning[45] reported a series of 437 patients with atrial arrhythmias in whom electrical cardioversion was attempted on 573 occasions: 228 patients were on long-term anticoagulant therapy, whilst 209 were not given anticoagulants. Thirteen patients (3%) experienced thromboembolic events, with two (1.1%) of the 186 patients in the anticoagulant group, compared to 11 (6.8%) of the 162 patients who were not on anticoagulants and were successfully cardioverted.[45] These results demonstrate that prior anticoagulant therapy was beneficial in attempted cardioversion. Furthermore, the advantageous effect of warfarin was apparent despite more patients with congestive heart failure, mitral valve disease, and hypertension (factors that increase the risk for thromboembolism) being present in the anticoagulated group. The thromboembolic events that did occur were predominantly noted 1–6 days following cardioversion, suggesting a 'high risk' period post-cardioversion.[45] However, this study was not randomised, and as patients were on chronic anticoagulant therapy, the value of short-term anticoagulant therapy could not be defined. In addition, this study included patients with atrial flutter and atrial tachycardia (in addition to atrial fibrillation), although the risk of thromboembolism in these subgroups has not been specifically defined.

In another retrospective study of 79 patients who underwent cardioversion, none of the 51 patients who received anticoagulant therapy had an embolic event, whilst two of 28 (7%) who were not anticoagulated had an embolic stroke.[47] Although the numbers are small, their results do support short-term anticoagulant treatment, especially in high-risk patients (defined in this study as patients aged $>55$ years, those with duration of atrial fibrillation $>1$ year, coronary artery disease, cardiomyopathy, or hypertension).[47]

More recently, Arnold *et al*[48] retrospectively assessed 454 elective direct current cardioversions performed for atrial fibrillation or atrial flutter over a seven-year period. The incidence of embolic complications was 1.32% (six patients); all of these patients had atrial fibrillation, none were on anticoagulants and the duration of atrial fibrillation was $<1$ week in five of them.[48] None of the patients with atrial flutter had thromboembolic events confirming the low thromboembolic risk for cardioversion of this subgroup of patients.

Whilst the above-mentioned studies were not randomised, the evidence for the beneficial effects of anticoagulant prior to cardioversion of atrial fibrillation, appears persuasive.

## NEW DEVELOPMENTS IN IDENTIFYING THOSE AT RISK OF THROMBOEMBOLISM

Although anticoagulation is relatively safe, effective anticoagulation is not

**Role of the general practitioner**

- identification of patients with new onset atrial fibrillation
- clinical assessment of thromboembolic risk* and the early initiation of antithrombotic therapy – warfarin will be required for most patients, whilst aspirin may be suitable for younger patients (age < 65 years) with no cardiac risk factors or structural heart disease
- assistance with monitoring of anticoagulant therapy
- referral of appropriate patients to a cardiologist for further assessment (including echocardiography) and consideration of cardioversion
- awareness of potential drug interactions and toxicity with anti-arrhythmic drugs and anticoagulants

*Three independent clinical predictors of an increased risk of stroke are a history of hypertension, recent (within three months) congestive heart failure, and previous cerebrovascular event (either stroke or transient ischaemic attack)

**Box 7**

completely free of a risk of bleeding complications. Clearly, it would therefore be advantageous to avoid unnecessary anticoagulation by the identification of 'high-risk' patients. New developments are the availability of transoesophageal echocardiography, and the availability of plasma prothrombotic markers which may assist management by detecting 'low risk' patients (perhaps by avoiding anticoagulation). In addition, evaluation of the possible efficacy of other methods of providing thromboprophylaxis, such as aspirin, in low-risk groups is required.

Transoesophageal echocardiography is superior to transthoracic echocardiography in detecting atrial thrombi, particularly in those involving the atrial appendage, and cardiac sources of thromboembolism.[40] For example, the sensitivity of transthoracic echocardiography for left atrial body and left atrial appendage thrombi has been reported as 78% and 35%, respectively.[49] Although the true sensitivity of transoesophageal echocardiography for detecting atrial thrombi is unknown, it is likely to be related to the size of the thrombus and the ability to obtain adequate imaging of the atria. It is accepted, however, that even embolisation of small thrombi may cause strokes and considerable morbidity. In a small series, early cardioversion was performed (in 78 patients) without long-term oral anticoagulant therapy (but with intravenous heparin for 24 hours), with no excess in embolic events.[40] By contrast, others have demonstrated that the exclusion by transoesophageal echocardiography of pre-existing thrombi before cardioversion did not eliminate the risk of thromboembolism.[35,42,50] A recent report also suggests that left atrial appendage thrombus on transoesophageal echocardiography is not uncommon in patients with acute-onset atrial fibrillation (< three days); and that the prevalence of thrombus in patients with recent emboli was comparable between patients with acute and chronic atrial fibrillation (21% *vs* 23%).[51] Larger trials on the use of transoesophageal echocardiography are still required, but for the present, it would probably be a useful investigation in patients in whom anticoagulation is especially hazardous. Thus, it is suggested that the role of transoesophageal echocardiography should be to enable early cardioversion (for example, duration of atrial fibrillation < 48 hours) if atrial thrombus is excluded and to identify high-risk patients with atrial thrombi, so as to postpone cardioversion and avoid the risks of thromboembolisation.[50]

Another advance would therefore be the identification of suitable prothrombotic markers, which could help in the risk stratification of patients pre- and post-cardioversion. Potential markers of thromboembolic risk include plasma fibrinogen and fibrin D-dimer (the latter as a marker of intravascular clotting) and abnormalities of such prothrombotic markers have been shown in atrial fibrillation.[36,37] One initial study of such markers post-cardioversion has demonstrated no significant differences in plasma fibrinogen levels, but a significant reduction in plasma fibrin D-dimer levels when pre-cardioversion levels are compared to levels 14 days post-cardioversion.[52]

The recent SPAF-II study has demonstrated that aspirin at a dose of 325 mg/day may be adequate thromboprophylaxis in certain low-risk subgroups of patients with nonvalvular atrial fibrillation.[53] As full anticoagulation with warfarin is not without risk and inconvenience, the question arises whether or not aspirin may be sufficient thromboprophylaxis for the cardioversion of 'low-risk' patients with atrial fibrillation. This is especially if a full pre-cardioversion risk assessment with transoesophageal echocardiography and prothrombotic markers is performed, and patients with a very low probability of thromboembolism can be identified.

## Other findings following cardioversion

Following cardioversion, alterations in left atrial size, ventricular function and transient electrocardiographic changes (including conduction disturbances and arrhythmias) may be encountered. In the initial stages, hypotension and bradycardia may also occur. Bradycardia is usually more common in patients with the sick sinus syndrome and following acute myocardial infarction.[54]

Cardiac output and exercise or functional capacity may be significantly improved following successful cardioversion to sinus rhythm.[3,4,55] These benefits may be due to a combination of a reduction in heart rate and the restoration of atrial systole. The former contributes to greater diastolic filling time, coronary flow, and reduced myocardial oxygen demand; whilst the latter contributes to increased ventricular filling.[3,56] The resumption of atrial systole may contribute to improved mitral and tricuspid valve closure with diminution of valvular insufficiency, resulting in improved cardiac performance.[56] There is also a reduction in left and right atrial sizes with the restoration of atrial systole.[34,57]

Full recovery of atrial mechanical activity may not, however, occur immediately following cardioversion, which may in part be due to atrial

'stunning' following the procedure.[35] The resumption of atrial activity may in fact be delayed despite the electrocardiogram showing immediate onset of sinus P waves.[33] In a pulsed Doppler evaluation of atrial mechanical function post-cardioversion, peak A wave velocity and per cent atrial contribution to total left ventricular filling did not return to normal until three weeks after cardioversion.[34] This finding may have implications for the onset of any clinical benefit (from the restoration of atrial systole) in patients with heart failure, and the delineation of any 'risk period' for thromboembolism (as, if atrial systolic function is still suboptimal, patients may continue to be at risk for atrial thrombus). A further study does suggest, however, that the degree of atrial mechanical activity following cardioversion may be very variable and embolic episodes are not necessarily related to this delayed return of atrial mechanical activity following cardioversion.[58]

The time course of the recovery of atrial systolic function may be related to the duration of atrial fibrillation before cardioversion. For example, full recovery of atrial systole is achieved within 24 hours in patients with recent onset (< two weeks) atrial fibrillation, whilst in those with prolonged (> six weeks) atrial fibrillation, atrial function takes up to four weeks to return.[59] As the restoration of atrial systole precedes the (late) improvement in left ventricular ejection fraction, it has been suggested that an intrinsic left ventricular cardiomyopathy is present in patients with atrial fibrillation.[4] Rarely, acute pulmonary oedema has been described following cardioversion, especially in patients with pre-existing left ventricular impairment.[5]

In general, arrhythmias post-cardioversion are due to either inadequate synchronisation or digoxin toxicity. The majority of these abnormal rhythms are atrial in origin and trivial. For example, premature beats and conduction disturbances (first or second degree AV block) are also common. Ventricular arrhythmias following cardioversion are less common but more serious. The most frequent of these is ventricular fibrillation, which may be induced in about 1% of cases but is usually treated by repeat shock.

In addition, post-cardioversion transient ST segment elevation may occur, usually related to previous pericardiotomy and age.[60] These ST segment changes were associated with an unfavourable arrhythmia prognosis, a lower conversion rate (48% *vs* 76% in those without these changes), and diminished long-term maintenance of sinus rhythm.[60] They do not, however, indicate myocardial infarction, although small rises in creatine kinase may occur with electrical cardioversion. The enzyme usually arises from skeletal muscle and myocardial damage is unlikely, which is confirmed by radionuclide studies.[61]

## Post-cardioversion management

Following successful cardioversion to sinus rhythm, it is important to continue with oral anticoagulants and possibly anti-arrhythmic therapy. The latter is to maintain sinus rhythm and prevent arrhythmia recurrence.

Current practice favours the maintenance of oral anticoagulation following cardioversion. The risk of thromboembolism probably continues despite successful cardioversion as atrial mechanical function may not be restored for several weeks.[33,45] The optimal duration or regime of anticoagulation is, as yet, unclear. Recent recommendations by the American College of Chest Physicians are summarised in box 8.[62] However, in patients who have a high risk of recurrent atrial fibrillation, it may be prudent to continue anticoagulation for longer than four weeks. However, the finding that left atrial appendage thrombus is relatively common even in acute-onset atrial fibrillation of less than three days' duration,[51] gives further impetus for early, full anticoagulation, starting with intravenous heparin (followed by warfarin) pending cardioversion.

Without anti-arrhythmic drugs, the risk of relapse of atrial fibrillation is high, with the proportion remaining in sinus rhythm ranging from 69% at one month to 58% at six months, 23% at a year and 16% at two years.[63,64] Maintenance of sinus rhythm post-cardioversion requires the use of anti-arrhythmic drugs that are similar to those used for pharmacological cardioversion, as discussed above. The sequential use of different types of anti-arrhythmic drugs may also improve arrhythmia prognosis in chronic atrial fibrillation or flutter after successful cardioversion.[65] For example, in a study of 127 patients undergoing cardioversion, serial drug treatment initially with flecainide (Stage I), followed by quinidine or sotalol if recurrence occurred (Stage II), and eventually amiodarone (Stage III), the two-year proportion of arrhythmia-free patients increased from 31% at Stage I to 63% at the end of serial treatment.[65] Anti-arrhythmic drugs should thus be considered post-cardioversion in patients at risk of recurrence of atrial fibrillation.

**Anticoagulation for cardioversion of atrial fibrillation**
(recommendations of the American College of Chest Physicians)[62]

- the administration of warfarin for three weeks before elective cardioversion of atrial fibrillation of $\geqslant$ 3 days' duration;
- continuation of warfarin therapy for four weeks after cardioversion;
- administration of intravenous heparin followed by warfarin if cardioversion cannot be postponed for three weeks; and
- no anticoagulant therapy for atrial fibrillation of $<$ 2 days' duration or for atrial flutter

**Box 8**

## Prognosis following cardioversion

Predictors of refractoriness to cardioversion or unsuccessful maintenance of sinus rhythm include the following: age, duration of arrhythmia, hypertension, valve disease, and other organic heart disease.

An older age, in combination with a large number of previous episodes of arrhythmia and a long duration of arrhythmia, were predictive of the unsuccessful maintenance of sinus rhythm.[65,66] In addition, the presence of coronary artery disease, hypertension and organic heart disease (such as mitral valve disease, aortic stenosis, and cardiomyopathy) are adverse factors for the maintenance of normal sinus rhythm following cardioversion.[33,66] In a Doppler echocardiographic study, a slow increase ($<10\%$ in first 24 hours) in the magnitude of A wave post-cardioversion was also predictive for the recurrence of atrial fibrillation.[67]

The effects of left atrial size are less certain. In a small study (50 patients), a left atrial dimension of $\geqslant$ 45 mm was important, and had a positive predictive value of $66\%$ for recurrence of atrial fibrillation.[68] However, recent studies have, in contrast, demonstrated the converse (that is, left atrial size does not appear to influence outcome following cardioversion).[63,66,68] In these studies, duration of atrial fibrillation was the most important predictor for outcome following cardioversion. These studies suggest therefore that atrial size does not strongly influence outcome of cardioversion and patients should not be excluded on these grounds from consideration of cardioversion. The increase in left atrial size may be consequent upon the presence of atrial fibrillation, which may explain why it does not necessarily predict outcome following cardioversion. Even in the

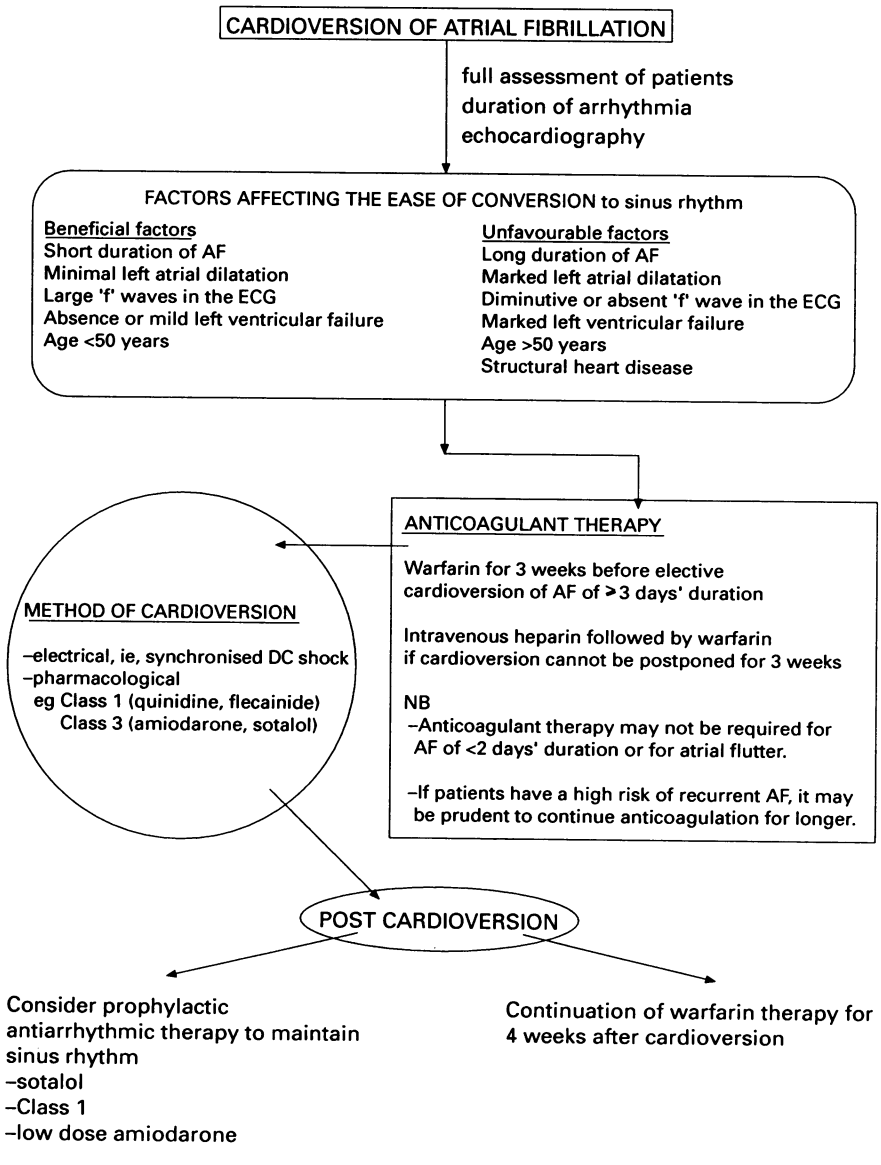


**Figure 2** Cardioversion of atrial fibrillation

**Summary/learning points**

- suitable patients with atrial fibrillation should be considered for cardioversion to sinus rhythm; this may have beneficial haemodynamic effects and a reduction in thromboembolic risk
- electrical or pharmacological methods may be effective
- Class I or Class III anti-arrhythmic drugs are the most effective agents for cardioversion and the maintenance of sinus rhythm
- post-cardioversion anti-arrhythmic therapy is most useful for the initial three months and is advisable in high risk patients, in view of the high relapse rate post-cardioversion
- anticoagulant therapy should be started 2–3 weeks prior to and continued for at least 4 weeks post-cardioversion

**Box 9**

presence of a dilated left atrium, long-term sinus rhythm (79% at 12 months) is possible with the use of anti-arrhythmic drugs.[68]

The duration of the arrhythmia is also an important factor influencing prognosis following cardioversion of atrial fibrillation. For example, there is a two-fold increase in the proportion remaining in sinus rhythm post-cardioversion when patients with a short duration of atrial fibrillation (less than three months) are compared with those in whom atrial fibrillation was present for more than 12 months.[33,63] However, the duration of atrial fibrillation alone should not be the sole basis for exclusion of such patients from cardioversion and many factors, such as the clinical state and the presence of structural heart disease should be considered.

Full assessment of the patient with atrial fibrillation for cardioversion should therefore include an assessment of the underlying aetiological factors(s). For example, patients with specific pathology (such as mitral stenosis and poor left ventricular function) are unlikely to cardiovert successfully. By contrast, a patient with atrial fibrillation secondary to thyrotoxicosis or a chest infection that has since been treated, would have a high success rate if cardioversion were attempted. If the underlying aetiology and triggering factor(s) continue to exert an effect, attempts at cardioversion may be unsuccessful and the therapeutic approach in such patients should be the use of anticoagulant therapy and 'rate control' of the ventricular response.

Thus, full cardiological assessment (including echocardiography) prior to cardioversion is important. Proper selection of patients suitable for the procedure and the use of anti-arrhythmic therapy to prevent recurrences of the arrhythmia will allow a more successful outcome (figure 2).

## Conclusion

Cardioversion to sinus rhythm should be considered for all suitable patients in atrial fibrillation in order to improve cardiac performance and to perhaps reduce the long-term risk of thromboembolic complications. Both pharmacological and electrical cardioversion are effective in restoring sinus rhythm, but the optimal use of prophylactic anti-arrhythmic therapy for maintaining sinus rhythm and the duration of post-cardioversion anticoagulant prophylaxis are important considerations.

Prophylactic post-cardioversion anti-arrhythmic therapy is advisable in 'high risk' patients in view of the high relapse rate post-cardioversion. Anticoagulant therapy begun before elective cardioversion is also advised although the most effective anticoagulation regimen (and duration of therapy) remains uncertain. The precise role of transoesophageal echocardiography and prothrombotic markers in the risk of stratification of the thromboembolic risk post-cardioversion needs to be further explored.

Thanks to Dr AP Rae and Dr MJ Metcalfe for their helpful comments during the preparation of this manuscript. The author is the recipient of the Edith Walsh and Ivy Powell Research Awards for cardiovascular disease from the British Medical Association.

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